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PRELIMINARY ASSESSMENT OF PREDICTIVE VALIDITY OF PERIARTICULAR BONE AREA AND SHAPE MARKERS IN KNEE OA

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Purpose: Changes in periarticular bone area and shape are well described in late stages of OA, but it is not known if these changes predict clinical and structural outcomes in knee OA. The objective of this study was to investigate if bone area and 3D shape changes over 24 months predict clinically relevant progression in knee OA over a 48 month follow-up period.
Methods: The OA Biomarkers Consortium undertook a nested case-control study of progressive knee OA within the Osteoarthritis Initiative (OAI), a unique longitudinal cohort with a publicly available repository of joint images, biospecimens and clinical profile data obtained at annual clinic visits. The case group (n=194) is defined by the combination of knee radiographic outcome (medial tibiofemoral joint space loss (mTF JSL) >= 0.7mm) AND symptom outcome (persistent worsening in WOMAC pain score, reaching a minimum clinically important threshold of 9 points on a 0-100 normalised scale), each achieved for the first time at the 24, 36 or 48 month follow-up compared to baseline. Main inclusion criteria were a Kellgren Lawrence grade (KLG) 1, 2 or 3 at baseline from central reading and availability of knee radiograph and magnetic resonance (MR) images at baseline and 24 months. Controls (n=406) were knees eligible for the study that did not meet both endpoint criteria consisting of: 200 subjects with no worsening on both factors (pain and mTF JSL), 103 subjects with JSN but no pain increase and 103 with a persistent increase in pain but no JSL. Femur, tibia and patella bone surfaces were automatically segmented from 3T DESS-we images using active appearance models provided by Imorphics (Manchester, UK), and built from an unrelated dataset. Two measures of change in bone shape from BL to 24 months were used as predictors (1) the change in tAB area on the medial and lateral femur, tibia and patella, and (2) the change in position on OA vectors for the femur, tibia and patella. The OA vector encodes the typical overall 3D shape difference between 300 knees with OA (KLG 3-4) and 300 without (KLG 0). A line is drawn through the two population means, and the 3D bone shape generated for each segmented bone surface is then projected orthogonally onto this OA vector. For the purposes of this analysis, we normalized all area and shape bone markers to a z scale. Association between bone shape markers and case-control status was assessed using a logistic regression model adjusting for baseline age, sex, BMI, KLG and baseline pain level. Additional analyses were conducted to detect marginal effects of bone markers on changes in pain and mTF JSL. To maintain overall type I error <0.05 the adjusted ORs were considered statistically significant if p<0.004.

Change in bone area (mm2) and shape (vector of 3D shape) for cases and controls

	means (SD) cases	means (SD) controls	Adjusted OR per 1SD	p-value p-value
Medial Femur	37.48(54.82)	16.13 (41.44)	1.64 (1.35, 1.99)	<0.0001
Medial Tibia	16.99 (22.11)	10.22 (19.14)	1.41 (1.18, 1.69)	0.0001
Medial Patella	7.25 (29.74)	3.10 (16.10)	1.30 (1.03, 1.62)	0.0252
Lateral Femur	7.98 (47.43)	0.45 (42.84)	1.23 (1.03, 1.48)	0.0255
Lateral Tibia	11.01(17.23)	5.53 (14.40)	1.46 (1.22, 1.75)	<0.0001
Lateral Patella	9.36 (37.41)	3.76 (21.21)	1.31 (1.04, 1.65)	0.0216
Notch	13.09(26.47)	6.22 (22.98)	1.32 (1.11, 1.58)	0.0022
Lateral Trochlea	7.09 (21.04)	0.57 (18.75)	1.41 (1.17, 1.69)	0.0002
Medial Trochlea	12.34 (14.55)	5.77 (11.24)	1.70 (1.41, 2.05)	<.0001
Vector Femur	0.30 (0.35)	0.16 (0.27)	1.65 (1.36, 1.99)	<.0001
Vector Tibia	0.35 (0.45)	0.22 (0.43)	1.39 (1.16, 1.66)	0.0003
Vector Patella	0.29 (0.68)	0.17 (0.68)	1.21 (1.01, 1.45)	0.0396

Results: By design cases and controls had similar age (mean 61.5 years, SD 8.9) and sex distribution with 59% female; the majority were obese (mean BMI 30.7 kg/m2). Changes in bone area and shape from BL to 24 months in all compartments were greater in cases compared to controls and, with the exception of the patella, significantly associated with an increased odds of being a case knee (Table 1). The adjusted ORs in the table represent the change in odds of being a 'case' per 1SD increase of normalized changes in area and shape bone markers. The odds ratios for area changes ranged from 1.24 to 1.73, and for changes in shape ranged from 1.21 to 1.65, with the largest ORs associated with bone changes in the medial femur and trochlea. Further analysis revealed that these associations were mediated by changes in JSL and not in pain.
Conclusions: Greater changes in bone area and shape markers over 24 months in knees with mild to moderate radiographic OA predict greater likelihood of progression over 48 months. This difference is largely explained on the basis of mTF JSL progression and not due to pain increases.

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MEDIAL MENISCAL PATHOLOGY INCREASES RISK OF INCIDENT RADIOGRAPHIC OSTEOARTHRITIS: A MATCHED CASE-CONTROL STUDY FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: Radiography is only able to depict structural joint damage at advanced stages. However, pre-radiographic structural damage to the joint is likely to increase the risk of incident radiographic OA (ROA). The menisci are crucial for preservation of joint integrity and meniscal damage alters joint biomechanics. Further, the menisci contribute to radiographic joint space narrowing, one of the hallmark features of ROA.
The aim of the study was to assess if presence and severity of meniscal damage and extrusion at the time point one year prior to the establishment of incident ROA (timepoint "P-1") increases the risk for incident ROA using a nested, matched case-control approach based on the Osteoarthritis Initiative (OAI) cohort focusing on cases of incident ROA with no evidence of ROA at baseline.
Methods: Participants were drawn from the OAI including 4796 participants with, or at risk of knee osteoarthritis. We studied 59 knees that developed incident ROA before the 48 month visit. They were matched with a control knee that did not develop incident ROA. All knees were from participants where both knees were KL = 0 at enrollment and matching was further done by gender and age within 5 years. MR images were acquired at four OAI clinical centers using Siemens Trio 3 T scanners.
MRIs were read for medial and lateral meniscal morphology using the semiquantitative MOAKS system, which scores meniscal morphology from 0 to 8. Morphology was scored for the following locations: anterior horn, body, posterior horn, medial and lateral. Grades 0 depicts a normal meniscus and grade 1 lesions are intrameniscal signal changes. Grades 2-5 code different types of meniscal tears while grades 6-8 code different grades of meniscal maceration. Extrusion was scored from 0-3 on coronal images according to MOAKS.
Conditional logistic regression was used to assess the risk of incident ROA based on the extent of meniscal damage and extrusion one year earlier (i.e. at P-1)
Results: Subjects were on average 65.5 years old (SD ± 8.6), predominantly female (58.1%) and overweight (mean BMI 29.5 SD ± 4.88).
Risk of incident ROA was significantly increased for knees exhibiting any pathology of the medial meniscal body at P-1 (OR=9.0 95% confidence interval [CI] [2.1,38.8]) and of the lateral posterior horn (OR=5.0 [1.1,22.8]) when compared to the knees with normal meniscal morphology as the reference. Knees with any medial extrusion exhibited an increased risk for incident OA when compared to knees without (Table 1).
Knees with a maximum meniscal grade of 2 or more (tear and maceration) in any of the 3 locations of the medial compartment had an increased risk for incident ROA (OR=19.4 [2.3,162.1]) when compared to knees with normal meniscal morphology (=grade 0).
Conclusions: Presence of any medial meniscal pathology and extrusion of the meniscal body predicts incident ROA one year later when compared to knees without these meniscal alterations. Further, risk for